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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,221	12/21/2001	Raghuram Kalluri	2312/2082B	3472

22204 7590 04/09/2007

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EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/032,221	KALLURI, RAGHURAM	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *108-117* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *108-117* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 3/22/07, is acknowledged.

2. Claims 108-117 are pending and under examination as they read on an isolated fragmetn of SEQ ID NO: 10 and SEQ ID NO: 37-42 as the species.

3. Applicant's IDS, filed 9/25/06, is acknowledged, however, the International Search Report was crossed out but the references listed thereon had been considered.

4. The amendment filed 11/08/04, stands objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: Applicant provides SEQ ID NO: 10 as 244 amino acids rather than 245 amino acid in the claimed provisional applications. However, the corresponding table legend to the sequences does not corresponding the sequence numbering. For example: T8: amino acids 68^{3}-94 of SEQ ID NO:39. In the table legend indicates for ^{3} in T8, lysine has been substituted for the leucine residue at position **69** of the full-length Tumstatin, however this position now is **68**.

Applicnat indicates the Preliminary amendment included some twenty-four pages of amendments to the specification and a thorough explanation demonstrating that the amendments conformed to the parent applications, corrected inadvertent errors, and did nto consitute new matter. Further, the Preliminary Amendment and subsequent Amendments to the specification have contained errors leading to the inconsistencies which the Examiner has pointed out as new matter. Applicant suggest that a substitute specification to correct sequence inflmation that would conform to the parent applications would solve the problem.

Accordingly, a substitute specification is required because the numerous entries to be amended in the specification, filed 10/18/02 and 11/08/04. The substitute specification filed must be accompanied by a statement that it contains no new matter. Such statement must be a verified statement if made by a person not registered to practice before the Office.

5. Claim 112 is objected to for the following informalities: the is extra ")," at line 3. correction is required.

6. Claims 109 and 114 are objected to because there is a discrepancy between the Sequence Listing of SEQ ID NO: 39 and the recited amino acid residues of SEQ ID NO: 39 at positions 77 and 81 of the full-length Tumstatin. The Sequence listing lists amino acid residue at position 77 as Leu while the claim recites the same residue at position 77 as Met. Further, residue 81 is listed in the Sequence Listing as Val while the claim recite the same residue as Ile, see below. Correction is required.

In claims 109 and 114:
Lys^{68} Gln^{69} Arg^{70} Phe^{71} Thr^{72} Thr^{73} Met^{74} Pro^{75} Phe^{76} Met^{77} Phe^{78} Cys^{79} Asn^{80} Ile^{81} Asn^{82} Asp^{83} Val^{84} Cys^{85} Asn^{86} Phe^{87} Ala^{88} Ser^{89} Arg^{90} Asn^{91} Asp^{92} Tyr^{93} Ser^{94}
In Sequence listing:
Lys^{68} Gln^{69} Arg^{70} Phe^{71} Thr^{72} Thr^{73} Met^{74} Pro^{75} Phe7^{6} Leu^{77} Phe^{78} Cys^{79} Asn^{80} Val^{81} Asn^{82} Asp^{83} Val^{84} Cys^{85} Asn^{86} Phe^{87} Ala^{88} Ser^{89} Arg^{90} Asn^{91} Asp^{92} Tyr^{93} Ser^{94}

6. Claims 110 and 115 are objected to because there is a discrepancy between the Sequence Listing of SEQ ID NO: 39 and the recited amino acid residues of SEQ ID NO: 40 at positions 81 of the full-length Tumstatin molecule. Residue 81 is listed in the Sequence Listing as Val while the claim recite the same residue as Ile, see below. Correction is required.

In claims 109 and 114:
Lys^{68} Gln^{69} Arg^{70} Phe^{71} Thr^{72} Thr^{73} Met^{74} Pro^{75} Phe^{76} Leu^{77} Phe^{78} **Ser**^{79} Asn^{80} Ile^{81} Asn^{82} Asp^{83} Val^{84} **Ser**^{85} Asn^{86} Phe^{87} Ala^{88} Ser^{89} Arg^{90} Asn^{91} Asp^{92} Tyr^{93} Ser^{94} (SEQ ID NO:40),

In Sequence listing:

Lys^{68} Gln^{69} Arg^{70} Phe^{71} Thr^{72} Thr7^{3} Met^{74} Pro^{75} Phe^{76} Leu^{77} Phe^{78} Ser^{79} Asn^{80} Val^{81} Asn^{82} Asp^{83} Val^{84} Ser^{85} Asn^{86} Phe^{87} Ala^{88} Ser^{89} Arg^{90} Asn^{91} Asp^{92} Tyr^{93} Ser^{94}

5. The following new ground of rejection is necessitated by the amendment submitted 3/22/07.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 108-117 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated, mutated Tumstatin polypeptide of SEQ ID NO: 10 comprising the following mutations:

A) wherein the Leu at position 77, Vla at postion 81 and Asp at position 83 have been substituted for Met, Ile and Asn, respectively,

B) wherein Leu at position 68 has been substituted for Lys,

C) wherein Leu at position 68, Cys at positions 79 and 85 have been substituted for Lys, Ser and Ser, respectively,

D) wherein Phe at position 76 and Asp at position 84 have been substituted for Lys and Cys, respectively, or

E) Leu at position 68, and Cys at positions 79 and 85 have been substituted to Lys, Asp and Asp, respectively, wherein said mutated polypeptide has the ability to inhibit angiogenic activity or the ability to inhibit protein synthesis in endothelial call, Or

An isolated Tumstatin polypeptide of SEQ ID NO: 10 having the amino acid sequence of SEQ ID NOS: 38-42, wherein said mutated polypeptide has the ability to inhibit angiogenic activity or the ability to inhibit protein synthesis in endothelial call

does not reasonably provide **enablement** for an isolated, mutated Tumstatin polypeptide "having" the amino acid sequence of SEQ ID NOS: 38-42, or fragment thereof, wherein the amino acid sequence of said fragment consists of SEQ ID NO: 45, wherein said polypeptide or fragment thereof, has the ability to inhibit tumor growth in claim 1, or has the ability to inhibit angiogenesis in claim 15, or an isolated mutated Tumstatin polypeptide of SEQ ID NO: 33, or a fragment thereof, wherein said fragment comprises SEQ ID NO: 45, wherein said polypeptide or fragment thereof further comprises one to five amino acid substitutions and has the ability to inhibit tumor growth in claim 6, or has the ability to inhibit angiogenesis in claim 20 or having the ability to inhibit protein synthesis in endothelial cells in claim 34 or an isolated Tumstatin fragment of SEQ ID NO: 33 or a fragment thereof comprising the amino acid sequence of SEQ ID NO: 45, and having the ability to inhibit protein synthesis in endothelial cells in claim 29. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

The term "mutated Tumstatin polypeptide" dose not limit the claims to the specific mutations recited in SEQ ID NOs: 38-42, but any mutation outside the claimed sequences as long as the polypeptide having the amino acids of SEQ ID NOs:38-42. It has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions can result in substantially different biological activities. Applicant has not enabled structurally related and unrelated compounds which would be expected to have difference in their activities. There is insufficient direction or objective evidence as to how to make and to how to use any Tumstatin mutants with the recited capability for the number of possibilities associated with the myriad of direct and indirect effects associated with various neural reflex pathways or molecules and, in turn, as to whether such a desired effect can be achieved or predicted, as encompassed by the claims. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the changes which can be made in the structure of Tumustatin mutants and still provide or maintain sufficient the claimed activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the

nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. No claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

March 30, 2007

Maher Haddad

Maher Haddad, Ph.D.
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